

Prediction of flu epidemic activity with dynamical model based on weather forecast

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Abstract

The seasonality of respiratory diseases (common cold, influenza, etc.) is a well-known phenomenon studied from ancient times. The development of predictive models is still not only an actual unsolved problem of mathematical epidemiology but also is very important for safety of public health. Here we show that SIRS (Susceptible-Infected-Recovered-Susceptible) model accurately enough reproduces real curves of flu activity. It contains variable reaction rate, which is a function of mean daily temperature.

The proposed alternation of variables represents SIRS equations as the second-order ODE with an outer excitation. It reveals an origin of such predictive efficiency and explains analytically the 1 : 1 dynamical resonance, which is known as a crucial property of epidemic behavior. Our work opens the perspectives for the development of instant short-time prediction of a normal level of flu activity based on the weather forecast, and allow to estimate a current epidemic level more precisely. The latter fact is based on the explicit difference between the expected weather-based activity and instant anomalies.

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1. Introduction

Seasonable variability of respiratory diseases such as flu or common cold is widespread and generally known phenomenon. It has been studied extensively in the last decade both theoretically and experimentally since complications of such “easy” diseases result in the pneumonia, pleurisy or death. There is a big trend in the mathematical epidemiology to develop models which allow to reproduce in details observed phenomenon (Altizer et al. (2006); Fisman (2007); Lofgren et al. (2007); Tamerius et al. (2011)) but it is not enough because the prediction of outbreaks is more important in this case.

The origin of seasonal epidemic variability has several reasons: social (seasonal variations in a contact rate, e.g. schooltime year schedule, which is important for a study of epidemics among children) (Altizer et al. (2006); Tamerius et al. (2011)) as well as meteorological (air temperature, humidity, illumination) conditions.

The comparative study of three factors such as minimal day temperature, relative humidity and cloud cover influencing respiratory diseases reflected in the Netherlands data (Meerhoff et al. (2009)) shows prevalent correlation with the minimal temperature. The presence of the correlation between this temperature and the relative humidity time series without a significant lag, the fact, which is natural for middle latitudes of Northern hemisphere, has been also demonstrated.

The statistical analysis evaluated recently with the epidemic data from Japan (Shoji et al. (2011)), Belgium, Portugal and the Netherlands (van Noort et al. (2012)) also does not show statistical dominance of absolute humidity over temperature as a controlling factor. Thus, one can choose only one of these two outer independent variables as a free parameter. Further, a temperature will be considered as this variable.

From the point of view of mathematical modeling of such systems, the mentioned seasonal effects are simulated by introduction of periodic coefficients into compartmental epidemiological models. However, the corresponding studies were devoted only to the stability analysis of mean basic reproduction number and abstract mathematical consideration of fixed points stability (Williams and Dye (1997); Rebelo et al. (2012)).

Some realistic models have been developed only within the last years. It can be noted minimal SIR (Susceptible-Infected-Recovered) model (van Noort et al. (2012)) with seasonal renewal of susceptible hosts, which is verified by the

comparison with real epidemiological data. This kind of seasonality (resetting of variables) was interpreted there as a result of relatively long-term factors, e.g. effect of antigenic drift and shift in viruses as well as vital dynamics in a population.

More realistic in the sense of continuity of the process is the SIRS (Susceptible-Infected-Recovered-Susceptible) model, which connects three kinds of individuals, susceptible (S), infected (I), and recovered (and temporally immune) (R) within the kinetic scheme



where $k(t)$ is a reaction rate, which could be time-dependent due to temperature variations; and there are characteristic times τ and θ describing the duration of illness and the period of temporal immunity.

The majority of works exploring epidemic oscillations within SIRS scheme deal with a probabilistic approach. The important result of stochastic (Markov chains) modeling of a temporal evolution (2)–(3) is the finding that large oscillations in the system are generated by the 1 : 1 dynamical resonance of intrinsic oscillations and sinusoidal oscillations of the parameter $k(t)$ (Dushoff et al. (2004)). Further, this fact was widely discussed in the context of a possible background for annual resonant forcing of epidemic oscillations (Fisman (2007); Lofgren et al. (2007)).

Particularly, the semiannual variation of $k(t)$ (winter/summer mean temperature), which replaces harmonic function used in (Dushoff et al. (2004)), satisfactory reproduces characteristic seasonal dynamics of influenza-like illness (ILI). It has been demonstrated in the recent study (Hooten et al. (2011)) based on the stochastic agent-based SIRS simulation and Bayesian framework for generating of resulting distributions, which were compared with USA data extracted from **Google Flu trends**.

However, the cited results of stochastic simulations remain, in principle, phenomenological observations but do not explain the origin of such resonant behaviour. Besides, in these papers, artificial or too averaged parameter variations have been considered that does not allow to analyze detailed interplay between microstructure of flu and temperature time series. Thus, the main goals of the present work are: i) to study analytically the mathematical background for the dynamical resonance basing on the ODE system corresponding

to the SIRS kinetic scheme (1)–(3) and ii) to demonstrate its potential for prediction of detailed flu activity using actual meteorological data.

2. Kinetic model

The system of ordinary differential equations, corresponding to the kinetic scheme (1)–(3) reads

$$\frac{dS}{dt} = -k(t)IS + \theta^{-1}R, \quad (4)$$

$$\frac{dI}{dt} = k(t)IS - \tau^{-1}I, \quad (5)$$

$$\frac{dR}{dt} = \tau^{-1}I - \theta^{-1}R. \quad (6)$$

Let us consider the simplest way to incorporate seasonal temperature variations $T(t)$ into the reaction rate $k(t) = k_0(1 + \kappa(t))$, namely, we define the variable part as the linear function $\kappa(t) = \kappa_0 T(t)/|T|_{max}$, where the positive constant $\kappa_0 < 1$.

To explore an ability of this approach to understand and predict real seasonal variations in the disease activity of ILI, we use data from **Google Flu Trends** via <http://www.google.org/flutrends/>, which are argued as a valid source for estimating flu activity (Ginsberg et al. (2009)). Note that it was also confirmed by the study of individual outbreaks by stochastic SIRS model (Hooten et al. (2011)). To avoid averaging over provinces, which are presented in this database, we consider data on flu activity in Berlin and Vienna. Thus, we consider data related to the averaging over the large cities, i.e. include the mixing of large well-localized population.

Both cities belong to European regions with the continental climate. The most typical example of influenza-like diseases is a common cold, which is a sufficiently continent-wide endemic seasonal illness. Therefore, a possible input into the experimental data of atypical flu-like diseases (such as new flu strains) could be negligible and ways of their geographical large-scale spread are out goals of this work. Thus, it is more preferable to neglect by the space variable and only to consider ODE equations for the modeling.

The daily mean temperature data series are taken from **European Climate Assessment & Dataset** (Klein Tank et al. (2002)) (<http://eca.knmi.nl/>) for stations Berlin-Tegel (ECA station code: 4005) and Wien (Vienna, ECA

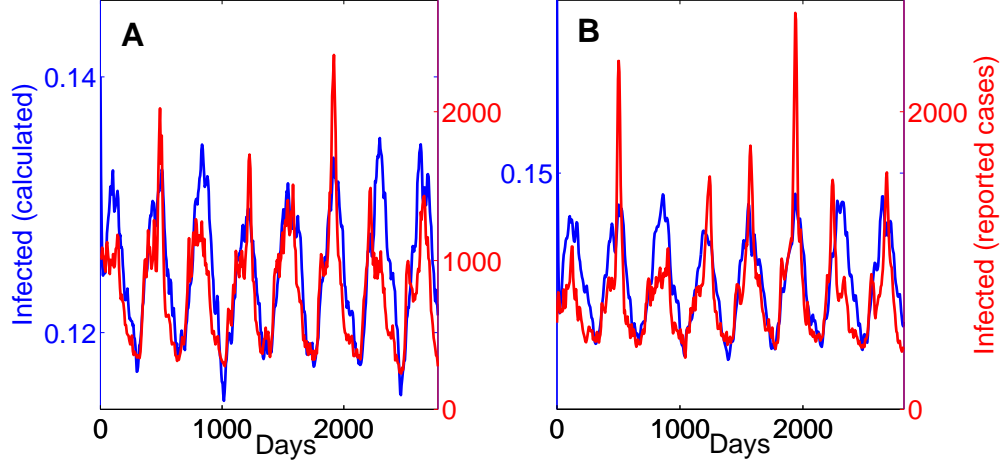


Figure 1: (Color online) Comparison of time series for calculated (dark-gray (blue online) lines) infected part of full population normed by unity and corresponding number of reported cases (light-gray (red online) lines) for Berlin (A) and Vienna (B). For both cities parameters of the model (4)–(6) are equal: $k_0 = 0.21$, $\kappa_0 = -0.07$, $\tau = 7$, $\theta = 10$; time intervals: October, 19, 2003 till May 22, 2011.

station code: 16), daily sampling. Results of numerical solutions of the system (4)–(6) with the substituted temperature-dependent reaction rate mentioned above are presented in the Fig. 1 in comparison with data series from Google Flu Trends.

Solution of the system (4)–(6) was evaluated by MATLAB R2006a routine `ode45` realizing the Runge-Kutta 4-5 method with the relative tolerance $1e - 7$, temperature values between sample's nodes were linearly interpolated. Calculations for linearized model (10) were evaluated using MATLAB routines for the Fast Fourier Transform.

One can see that the numerical simulation of the model sufficiently good reproduces actual flu activity for both considered samples. First of all, the simulated oscillations are undamped and one can note the high accuracy of coincidence of periods for measured and simulated curves. This clearly indicates that the used temperature variations enforce the desired oscillations.

But even more important is the coincidence of not only periods but also shapes of curves, especially in the minima of each period's magnitude. One can clearly see that even small saw-like details overlap for many lower parts of both real and simulated curves in the Fig. 1.

Table 1: Correlation coefficients for the pairwise real and simulated oscillating time series presented in the Fig. 1

City	Correlation coefficients for sequential individual periods							for total time
Berlin	0.89	0.84	0.82	0.89	0.85	0.70	0.77	0.78
Vienna	0.69	0.83	0.77	0.83	0.82	0.53	0.75	0.70

Apart of visual comparison, let us provide some quantitative statistical results on flu data and their temperature-based simulation shown in the Fig. 1. Table 2 presents total correlation coefficient for both curves over all period of simulations as well as correlation coefficients for each period of oscillatory flu outbreaks. To determine these short-time correlation coefficients, full time interval is subdivided into parts corresponding to unique individual periods of oscillations. Their boundary points are determined as time moment of cross-section of the curve presenting **Google Flu** data and the median line for the data. The starting point for each subinterval is chosen in top-down cross-section point. As a result, the correlation coefficients are determined for experimental and calculated time series located between closest subdivision points.

One can see that correlation coefficient is larger within majority of these subintervals than for the distributions taken for the whole interval. This fact principally originates from the epidemic outbreak within the 6th full period of oscillations for both cities. The values of most of the other coefficients argue that not only period of oscillations are the same but and their shape is sufficiently correlated even for such simple model. This also answers the question about other seasonal factors (like school vacation): the correlation coefficient of the model temperature-dependent solution and the real data are even higher within most of individual seasons then averaged over many seasons periodicity. Correspondingly, the temperature dependence could be considered as a leading factor.

This confirms the point of view that there exists a natural level of seasonal flu activity, which is principally determined by the variation of a daily mean air temperature. At the intermediate level of activity, this direct influence can also be traced: there are the same shape details, however some time they shifted relative to each other. These displacements can be explained by the presence of irregular temporary localized outbreaks, which

depend on a variety of factors (social, virological, etc). These factors play a major role at highest levels of flu activity. That is why, the several seasonal maxima differ from weather-based prediction being connected with an actual epidemiological situation.

To reveal the origin of a resonant behaviour, let us apply the co-ordinate transformation providing more explicit representation of a forcing. First of all, the system (4)–(6) is actually two-dimensional due to the conservation law $S + I + R = 1$. It is more convenient to introduce new variable $N = \tau^{-1}I - \theta^{-1}R$ that extremely reduces the Eq. (6), denoting N simply as a time derivative of R .

For the constant reaction rate $k = k_0 = \text{const}$ the standard procedure shows that the ODE system with respect to variables (N, R) has a non-trivial stationary point

$$N_s = 0, \quad R_s = \frac{1 - \tau^{-1}k_0^{-1}}{1 + \tau\theta^{-1}}. \quad (7)$$

Linear analysis with respect to N , $r = R - R_s$ declares that $(0, R_s)$ is a stable focus. In other words, any small deviation from $(0, R_s)$ decays oscillatory with the intrinsic frequency $\omega_i = [\omega_0^2 - (\lambda/4)^2]^{1/2}$, where $\lambda = \tau^{-1} + \theta^{-1} + R_s k_0 [1 + 2\tau\theta^{-1}] - k_0$ and $\omega_0 = \theta^{-1/2} (k_0 - \tau^{-1})^{1/2}$.

Thus, considering a general time-dependent reaction rate $k(t) = k_0[1 + \kappa(t)]$, $|\kappa| < 1$, it is possible to represent the Eqs. (6)–(4) in the form

$$\begin{aligned} \frac{dr}{dt} &= N, \\ \frac{dN}{dt} &= R_s \theta^{-1} \tau^{-1} \kappa(t) - \\ &\quad (\tau^{-1} + \theta^{-1} + R_s k(t) [1 + 2\tau\theta^{-1}] - k(t)) N - \theta^{-1} (k(t) - \tau^{-1}) r - \\ &\quad k(t) \tau N^2 - k(t) (1 + \tau\theta^{-1}) N r - k(t) \theta^{-1} [1 + \tau\theta^{-1}] r^2. \end{aligned} \quad (8)$$

This form allows to discuss influence of a reaction rate variability in a most explicit way. First of all, the first term in the left-hand side of the Eq. (9) demonstrates that the variability of the reaction rate corresponds actually to an external time-dependent excitation. This means that resonant properties of the solution for SIRS equations have primarily outer-, not parametric resonance origin in this case. And this result accomplishes for perturbations arbitrary strength and functional character (the case of small harmonic $\kappa(t)$ will be considered and discussed below).

The linear (second line in the Eq. (9)) and non-linear (third line in the Eq. (9)) terms include time-varying $k(t)$ as well. Therefore, in the case of sufficiently large $\kappa(t)$, some parametric excitation could be detected too. However, due to positivity of fixed parameters and their range resulting in both positivity of R_s and strong decay of free outbreaks, these inner effects are as a rule smaller then outer ones.

Finally, the realistic conditions $N \ll 1$, $r \ll 1$ (number of individuals on various stages of illness is sufficiently smaller than a full population) provides an opportunity to neglect by non-linear terms in the Eq. (9) for the case of steady oscillatory regime and for $|\kappa| \ll 1$ to neglect its variation in the second line of the Eq. (9). Under these assumptions, the system (8)–(9) reduces to the simple standard linear second order ordinary differential equation. It should be noted that the mathematically similar system has been obtained by K. Dietz (Dietz (1976)) in the problem of another epidemiological origin: endogenous diseases with vital dynamics and restriction to the simple harmonic variation of reaction rate.

For this reason, we neglect by the non-linear terms (the third line in the Eq. (9)) and variable parts of $k(t)$ in the linear ones (the second line in the Eq. (9)) as small quantities. Thus, the rest expression is a simple non-homogeneous harmonic ODE and the resulting solution for the number of infected individuals reads as

$$I = \tau\theta^{-1}R_s + \kappa_0 \frac{R_s\theta^{-1}}{2\pi} \int_{-\infty}^{+\infty} \frac{\theta^{-1} + i\omega}{[\omega_0^2 - \omega^2] + i\omega\lambda} \hat{\kappa}(\omega) d\omega, \quad (10)$$

where $\hat{\kappa}(\omega)$ is a Fourier transform of time series for a normed mean temperature.

The formula (10) explains the phenomena of 1 : 1 dynamical resonant excitation for sinusoidal (Dushoff et al. (2004)) and stochastic (Black and McKane (2010)) perturbations of the reaction rate since the integral kernel has a form of resonant filter, which amplify the spectral component coinciding with the intrinsic frequency of oscillations. In more general case, this kernel reshapes time series of temperature oscillations into time series of flu activity. The illustration of this procedure is presented in the Fig. 2.

Considering Fig. 2A, one can see that the spectrum of reported flu activity has two prevailing peaks corresponding to the first and second harmonics of time series and relatively fast decay elsewhere. The temperature spectrum has main harmonics located in the same place (however with smaller amplitude) and a thicker tail, which take over a significant part of spectral density.

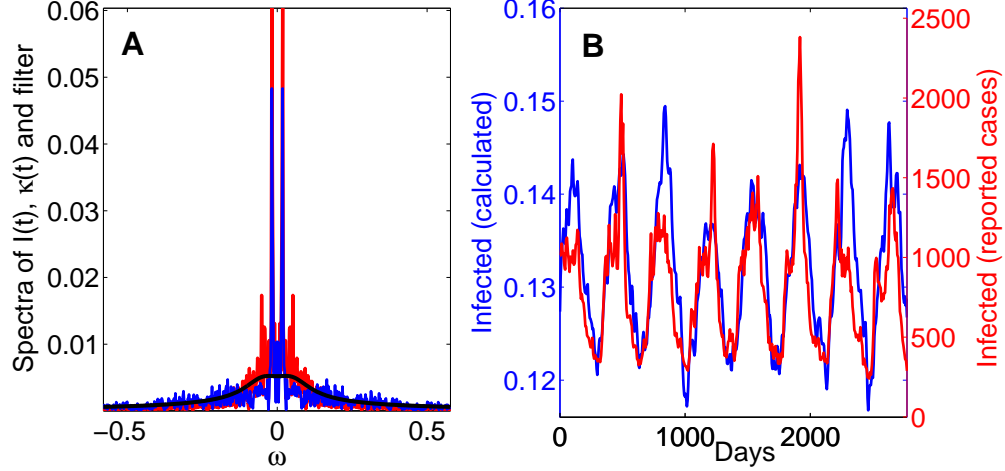


Figure 2: (Color online) A) Normalized to unit area under curves, absolute values for spectra of daily mean temperature (dark-gray (blue online) curve), reported flu activity (light-gray (red online) curve) and resonant filter (black curve). B) Comparison of calculated via the expression (10) (dark-gray (blue online) curve) and actually reported (light-gray (red online) curve) common flu activity in Berlin. The parameters of the model are the same as in the Fig. 1.

Thus, the harmonic filter in the Eq. (10), which is drawn as the black line in the Fig. 2, boosts the central part of temperature spectrum providing its better coincidence with the flu activity spectrum. This results in a rather good reproduction of flu activity curve, see Fig. 2B even in this simplified linearized case. Moreover, comparison of Figs 2B and 1A shows their high similarity in a shape. Thus, this indicates that harmonic filtering (10) is the actual governing factor, which determines seasonal flu activity through temperature seasonality.

3. Summary and outlooks

In this work, we show that seasonal mean temperature variation determines principal activity of influenza-like diseases and the latter can be calculated basing on the classical SIRS model with the variable temperature-dependent reaction rate.

The proposed method can be used for an instant short-time prediction of local level influenza-like illnesses basing on current epidemiological level and weather forecast. Current activity data (instant short-time sample) allow to

adjust parameters of SIRS ODE system and initial conditions. This equation should be solved numerically with the variable reaction rate, which incorporates temperature time series obtained from a weather forecast. The result provides prediction of a “normal” (weather-based) flu activity for nearest days (up to a decade). It should be pointed out that a definition of this “normal level of epidemiological activity” is the question, which is discussed from times of birth modern mathematical epidemiology, see e.g. (Hedrich (1927)) up to now, see e.g. the review (Stephenson and Zambon (2002)).

Our approach allows to refine this definition via a replacement of pure averaging over a long time interval with the instant value. This will allow avoid misinterpretation of a danger of new respiratory virus strain since the instant temperature anomalies can result in lower or higher levels of outbreak. Anomalies calculated as a difference between observed and expected temperature-based flu activity will give more reasoned alarms.

Thus, the proposed model has a predictive power and opens perspectives for future detailed research for a variety of world’s regions. Further, it allows developing technological (say, web-based) forecast applications.

Finally, it should be noted that the studied system belongs to the wide class of ODEs applicable to various problems of physical chemistry and biophysics. Thus, the obtained results could be used for the search of new approaches to a parametric control in autocatalytic systems that is a permanent interest of non-linear dynamics.

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